REMARKS

In the Office Action dated July 11, 2005, the Examiner has withdrawn the previous Restriction Requirement in view of Applicants' remarks and in favor of the following new Restriction Requirement. Specifically, the Examiner contends that this application contains the following groups of inventions that are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I	Claims 1-21, 29, 30 and 43, drawn to a compound which interacts with the β-amyloid peptide and a composition.
Group II	Claims 22-28, drawn to a method of selecting or designing a compound which inhibits the binding of metal ions to the N-terminus of the β-amyloid peptide.
Group III	Claims 31-42 and 44, drawn to a method of inhibiting the binding of one or more metal ions to the β-amyloid peptide and a method of preventing, treating, or alleviating Alzheimer's disease.

The Examiner states that Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, Groups I-III lack the same or corresponding special technical features. Specifically, the Examiner states that the technical feature of Group I is "a compound that interacts with the β-amyloid peptide", which, according to the Examiner, does not constitute a contribution over the art. In this connection, the Examiner refers to Shao, et al. (*J. Molecular Biol.* 285: 755-773, 1999), page 767, where it is stated that, "[a]s for the nicotine-inhibition to β-amyloidosis, the NMR work established that nicotine binds to the His13 and His14 side-chains of the Tyr10-Val24 α-helix, and this prevented an α-helix → β-sheet conversion and β-amyloid precipitation." Thus, it is Examiner's position that binding of nicotine to β-amyloid protein at His13 and His14, as disclosed by Shao et al., inherently "blocks" the N-terminus in such a way that binding of metal ions at said His residues is inhibited. The

Examiner therefore concludes that the technical feature of Group I does not make a contribution over the prior art, and thus, Groups I-III cannot be unified by a special technical feature.

Furthermore, the Examiner states that the application contains claims directed to more than one species of the generic invention. Specifically, the Examiner contends that the claims are generic to a myriad of compounds that interact with the β-amyloid peptide, including those identified in the schemes, tables, and figures of the specification. The Examiner has required Applicants to elect a single species to which the claims will be restricted if no generic claim is finally held to be allowable.

In order to be fully responsive to the Examiner's requirements for restriction, Applicants provisionally elect to prosecute the subject matter of Group III, claims 31-42 and 44, drawn to a method of inhibiting the binding of one or more metal ions to the β-amyloid peptide and a method of preventing, treating, or alleviating Alzheimer's disease. Further, in response to the requirement for species election, Applicants elects the compound BR7158 (described on page 26). Claims 31-42 and 44 all read on the elected species. Applicants reserve the right to file one or more divisional applications to pursue the non-elected subject matter. However, Applicants hereby traverse the Examiner's requirement for restriction and request reconsideration thereof in view of the following remarks.

A requirement for restriction presupposes an analysis of the subject application in light of the rules governing this practice, i.e., 37 C.F.R. §1.499 and PCT Rules 13.1 and 13.2. PCT Rule 13.1, first sentence, states: "The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ('requirement of unity of invention')." (Emphasis added.) PCT Rule 13.2 states: "The expression "technical features' shall mean those technical features that define a contribution

which each of the claimed inventions, considered as a whole, makes over the prior art." (Emphasis added.)

Applicants respectfully submit that unity of invention is the issue at hand. Applicants should be given the opportunity to argue on the merits during prosecution as to whether the claims are novel relative to the referenced prior art. Restriction of the claims based on an allegedly anticipating reference would deny Applicants such an opportunity. Furthermore, Applicants respectfully submit that the International Search Report has not raised any issues on the basis of lack of unity of invention.

Furthermore, Applicants respectfully submit that the present application is predicated in part on the determination that zinc and copper bind predominantly to a region in the N-terminal loop of Aβ that includes a cluster of histidine residues. This unique recognition provides the basis for the rational design or selection of inhibitors of the binding of zinc, copper and/or iron to Aβ. It is noted that the disclosure of Shao is limited to nicotine binding to Aβ. Shao does not teach or suggest design or selection of inhibitors of the binding of zinc, copper and/or iron to Aβ, or any compounds made or identified on this basis. As a result of the ability to block binding by metal ions to Aβ, the compounds designed or selected in accordance with the present invention are useful for treating diseases such as Alzheimer's disease. Therefore, it is respectfully submitted that all claims presented in the pending application are directed to the design, making and use of compounds that inhibit the binding of metal ions to Aβ at identified residues or regions of Aβ, thereby inhibiting the aggregation of Aβ, which is useful for treating conditions such as Alzheimer's disease. It is submitted that the present claims are so linked as to form a single general inventive concept, and should be examined in the same application. At the very least, Applicants respectfully submit that Group II, drawn to methods of design and

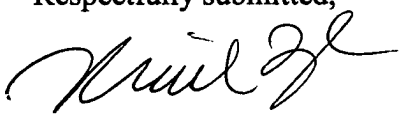
selection of relevant compounds, and Group III, drawn to therapeutic methods by employing the relevant compounds, should be examined together.

With respect to the species election, it is respectfully submitted that the compounds contemplated for use in the claimed methods share the common feature of inhibiting the metal ions, such as zinc and copper, to bind to Aβ. It is recognized that the claims will be restricted to the elected species only if the Examiner determines that the generic claims are not allowable.

Finally, Applicants respectfully submit that a determination to make the pending restriction requirement final must evidence the patentable distinctness of all defined three groups, one from the other, as presented by the Examiner.

Accordingly, it is respectfully submitted that the present application satisfies the requirements for unity of invention. Applicants respectfully urge that the Examiner reconsider and withdraw the requirement for restriction and provide an action on the merits with respect to all the claims.

Respectfully submitted,



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